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********** STN Columbus **********

FILE 'HOME' ENTERED AT 15:06:12 ON 17 FEB 1999

=> file medline cancerlit scisearch biosis embase wpids

FILE 'MEDLINE' ENTERED AT 15:06:39 ON 17 FEB 1999

FILE 'CANCERLIT' ENTERED AT 15:06:39 ON 17 FEB 1999

FILE 'SCISEARCH' ENTERED AT 15:06:39 ON 17 FEB 1999
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FILE 'BIOSIS' ENTERED AT 15:06:39 ON 17 FEB 1999
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FILE 'WPIDS' ENTERED AT 15:06:39 ON 17 FEB 1999
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=> set plurals on

     COMMAND COMPLETED

=> s hemochromatosis

L1      11342 HEMOCHROMATOSIS

=> s l1 and MHC

L2        252 L1 AND MHC

=> s l2 and alpha-2

  2 FILES SEARCHED...
  4 FILES SEARCHED...
L3          7 L2 AND ALPHA-2

=> dup rem

ENTER L# LIST OR (END):l3

PROCESSING COMPLETED FOR L3
L4          5 DUP REM L3 (2 DUPLICATES REMOVED)

=> d l4 1-5 ibib ab


L4  ANSWER 1 OF 5  SCISEARCH  COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER:   1998:795745  SCISEARCH
THE GENUINE ARTICLE: 127GV
TITLE:              Genomics, isoforms, expression, and phylogeny of the
                    MHC class I-related MR1 gene
AUTHOR:             Riegert P; Wanner V; Bahram S (Reprint)
CORPORATE SOURCE:   CTR RECH IMMUNOL & HEMATOL, 4 RUE KIRSCHLEGER, F-67085
                    STRASBOURG, FRANCE (Reprint); CTR RECH IMMUNOL & HEMATOL,
                    F-67085 STRASBOURG, FRANCE; BASEL INST IMMUNOL, BASEL,
                    SWITZERLAND
COUNTRY OF AUTHOR:  FRANCE; SWITZERLAND
SOURCE:             JOURNAL OF IMMUNOLOGY, (15 OCT 1998) Vol. 161, No. 8, pp.
                    4066-4077.
                    Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE,
                    BETHESDA, MD 20814.
                    ISSN: 0022-1767.
DOCUMENT TYPE:      Article; Journal
FILE SEGMENT:       LIFE
LANGUAGE:           English
REFERENCE COUNT:    66
                    *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB  A growing number of non-MHC-encoded class I-related molecules have been shown to perform diverse, yet essential, functions, These include T cell presentation of bacterially derived glycolipidic Ags by CD1, transcytosis of maternal IgG by the neonatal Fc receptor, enriched presence and plausible function within exocrine fluids of the Zn-alpha(2)-glycoprotein, subversion of NK cytolytic activity by the CMV UL18 gene product, and, finally, crucial involvement in iron homeostasis of the HFE gene. A recently described member of this family is the MHC class-I related (MR1) gene. The most notable feature of MR1 is undoubtedly its relatively high degree of sequence similarity to the MHC-encoded classical class I genes. The human chromosome 1q25.3 MR1 locus gives rise not only to the originally reported 1,263-bp cDNA clone encoding a putative 341-amino acid polypeptide chain, but to many additional transcripts in various tissues as well. Here we define the molecular identity of all human and murine MR1 isoforms generated through a complex scenario of alternative splicing, some encoding secretory variants lacking the Ig-like alpha 3 domain, Moreover, we show ubiquitous transcription of these MR1 variants in several major cell lineages. We additionally report the complete 18,769-bp genomic structure off the MR1 locus, localize the murine orthologue to a syntenic segment of chromosome I, and provide evidence for conservation of a single-copy MR1 gene throughout mammalian evolution. The 90% sequence identity between the human and mouse MR1 putative ligand binding domains together with the ubiquitous expression of this gene favor broad immunobiologic relevance.

L4  ANSWER 2 OF 5  SCISEARCH  COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER:   1998:793658  SCISEARCH
THE GENUINE ARTICLE: 127TU
TITLE:              Expanded genomic organization of conserved mammalian
                    MHC class I-related genes, human MR1 and its
                    murine ortholog
AUTHOR:             Yamaguchi H; Kurosawa Y; Hashimoto K (Reprint)
CORPORATE SOURCE:   FUJITA HLTH UNIV, INST COMPREHENS MED SCI, TOYOAKE, AICHI
                    47011, JAPAN (Reprint); FUJITA HLTH UNIV, INST COMPREHENS
                    MED SCI, TOYOAKE, AICHI 47011, JAPAN
COUNTRY OF AUTHOR:  JAPAN
SOURCE:             BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (29
                    SEP 1998) Vol. 250, No. 3, pp. 558-564.
                    Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525
                    B ST, STE 1900, SAN DIEGO, CA 92101-4495.
                    ISSN: 0006-291X.
DOCUMENT TYPE:      Article; Journal
FILE SEGMENT:       LIFE
LANGUAGE:           English
REFERENCE COUNT:    52
                    *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB  MR1 is a major histocompatibility complex (MHC) class I-related gene located outside the human MHC. Among several divergent class I molecules, the predicted MR1 molecule is closest, in the alpha 1 and alpha 2 domains, to the class I group to which the vertebrate classical class I molecules belong. We report here the genomic organizations of the human MR1 and mouse MR1 genes. Both genes exhibit genomic structures largely similar to those of the MHC class I genes. However, they are highly expanded in their scale in contrast to the classical MHC class I genes. Inclusion of transposable elements into introns seems to partly contribute to these genomic structures. Several other MHC class I-related genes also show relatively large genomic structures. The present study extended heterogeneity in the genomic organization among the class I gene family by revealing a highly expanded structure of the human MR1 gene and its murine ortholog. (C) 1998 Academic Press.

L4  ANSWER 3 OF 5  MEDLINE                    DUPLICATE 1
ACCESSION NUMBER:   1998225335  MEDLINE
DOCUMENT NUMBER:    98225335
TITLE:              Hemochromatosis and iron needs.
AUTHOR:             Halliday J W
CORPORATE SOURCE:   Queensland Institute of Medical Research, Bancroft Centre,
                    Royal Brisbane Hospital, Queensland, Australia.
SOURCE:             NUTRITION REVIEWS, (1998 Feb) 56 (2 Pt 2) s30-7; discussion
                    s54-75. Ref: 41
                    Journal code: OAY. ISSN: 0029-6643.
PUB. COUNTRY:       United States
                    Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           English
ENTRY MONTH:        199807
ENTRY WEEK:         19980704
AB  Although iron is an essential dietary requirement, the amount absorbed by the body is well regulated and depends on body iron stores and on dietary iron availability. There is very little iron excreted under normal conditions. Iron deficiency is a worldwide problem but iron overload, as seen in the inherited disease, hemochromatosis, is a major cause of morbidity in some Caucasian populations. This is a problem particularly where there is an adequate dietary iron intake and especially in males. A mutation has recently been described in an MHC Class I-like gene (HFE) that encodes for a protein (HFE) of 343 amino acids. The molecule contains a signal sequence peptide-binding region, alpha, and alpha(2) domains, and an immunoglobulinlike alpha(3) domain, in addition to a transmembrane region and a small cytoplasmic tail. It is a candidate gene for hemochromatosis. Several possibilities as to the function of this gene and the corresponding protein have been suggested but none has yet been confirmed. The mutation has been detected by several different groups in 80%-100% of subjects with the disease. However, in one study, 18%-20% of patients with the mutation did not exhibit significant iron overload. The discovery of this gene has important implications for both clinical studies and the elucidation of the pathways of iron metabolism.

L4  ANSWER 4 OF 5  EMBASE  COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   1998128551  EMBASE
TITLE:              Hemochromatosis and iron needs.
AUTHOR:             Halliday J.W.
CORPORATE SOURCE:   Dr. J.W. Halliday, QLD Institute of Medical Research, The
                    Bancroft Centre, PO Royal Brisbane Hospital, Brisbane, QLD
                    4029, Australia
SOURCE:             Nutrition Reviews, (1998) 56/2 II (S30-S37).
                    Refs: 41
                    ISSN: 0029-6643 CODEN: NUREA8
COUNTRY:            United States
DOCUMENT TYPE:      Journal; Conference Article
FILE SEGMENT:       029  Clinical Biochemistry
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB  Although iron is an essential dietary requirement, the amount absorbed by the body is well regulated and depends on body iron stores and on dietary iron availability There is very little iron excreted under normal conditions. Iron deficiency is a worldwide problem but iron overload, as seen in the inherited disease, hemochromatosis, is a major cause of morbidity in some Caucasian populations. This is a problem particularly where there is an adequate dietary iron intake and especially in males. A mutation has recently been described in an MHC Class I-like gene (HFE) that encodes for a protein (HFE) of 343 amino acids. The molecule contains a signal sequence peptide-binding region, .alpha.1 and . alpha.2 domains, and an immunoglobulin-like .alpha.3 domain, in addition to a transmembrane region and a small cytoplasmic tail. It is a candidate gene for hemochromatosis. Several possibilities as to the function of this gene and the corresponding protein have been suggested but none has yet been confirmed. The mutation has been detected by several different groups in 80%-100% of subjects with the disease. However, in one study, 18%-20% of patients with the mutation did not exhibit significant iron overload. The discovery of this gene has important implications for both clinical studies and the elucidation of the pathways of iron metabolism.

L4  ANSWER 5 OF 5  BIOSIS  COPYRIGHT 1999 BIOSIS      DUPLICATE 2
ACCESSION NUMBER:   1997:87562  BIOSIS
DOCUMENT NUMBER:    PREV199799379275
TITLE:              Identification of a mouse homolog for the human hereditary
                    hemochromatosis candidate gene.
AUTHOR(S):          Hashimoto, Keiichiro (1); Hirai, Momoki; Kurosawa, Yoshikazu
```

CORPORATE SOURCE: (1) Inst. Comprehensive Med. Sci., Fujita Health Univ.,
Toyoake, Aichi 470-11 Japan
SOURCE: *Biochemical and Biophysical Research Communications,* (1997)
Vol. 230, No. 1, pp. 35-39.
ISSN: 0006-291X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Recently, a novel human major histocompatibility complex (**MHC**) class I-like gene (HLA-H) was reported as a candidate gene for human hereditary haemochromatosis, a recessive disease of iron metabolism with a remarkably high incidence in northern Europeans. Independently we have isolated this gene in the course of a search for new human **MHC** *class I-related genes and named it MR2.* Here we report a mouse homolog of this human gene. The mouse MR2 gene is similar to the human counterpart with an overall predicted amino acid sequence similarity of apprx 66% and it is expressed *in various tissues as in human. The extra eight amino acid* residues between the a1 and the **alpha-2** domains in the mouse molecule compared to the human counterpart can be explained by the creation of the coding sequence from the intron. While the human gene is located at the site telomeric to the **MHC** region on human chromosome 6, our study indicated the translocation of the mouse homolog from the site telomeric to the **MHC** on mouse chromosome 17 to *chromosome 13 along with other genes.* This mouse gene should be important in clarifying a possible role in iron metabolism.

=> s l2 and alpha-3

2 FILES SEARCHED...
5 FILES SEARCHED...
L5 4 L2 AND ALPHA-3

=> dup rem

ENTER L# LIST OR (END):l5

PROCESSING COMPLETED FOR L5
L6 3 DUP REM L5 (1 DUPLICATE REMOVED)

=> d l6 1-3 *ibib ab*

L6 ANSWER 1 OF 3 SCISEARCH *COPYRIGHT 1999 ISI (R)*
ACCESSION NUMBER: 1998:795745 SCISEARCH
THE GENUINE ARTICLE: 127GV
TITLE: Genomics, isoforms, expression, and phylogeny of the **MHC** class I-related MR1 gene
AUTHOR: Riegert P; Wanner V; Bahram S (Reprint)
CORPORATE SOURCE: CTR RECH IMMUNOL & HEMATOL, 4 RUE KIRSCHLEGER, F-67085
STRASBOURG, FRANCE (Reprint); CTR RECH IMMUNOL & HEMATOL,
F-67085 STRASBOURG, FRANCE; BASEL INST IMMUNOL, BASEL,
SWITZERLAND
COUNTRY OF AUTHOR: FRANCE; SWITZERLAND
SOURCE: JOURNAL OF IMMUNOLOGY, (*15 OCT 1998*) Vol. 161, No. 8, pp.
4066-4077.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE,
BETHESDA, MD 20814.
ISSN: 0022-1767.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 66
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A growing number of non-**MHC**-encoded class I-related molecules have been shown to perform diverse, yet essential, functions, These include T cell presentation of *bacterially derived glycolipidic Ags by* CD1, transcytosis of maternal IgG by the neonatal Fc receptor, enriched presence and plausible function within exocrine fluids of the Zn-alpha(2)-glycoprotein, subversion of NK cytolytic activity by the CMV UL18 gene product, and, finally, crucial involvement in iron homeostasis of the HFE gene. A recently described member of this family is the **MHC** class-I related (MR1) gene. The most notable feature of MR1 is undoubtedly its relatively high degree of sequence similarity to the **MHC**-encoded classical class I genes. The human chromosome 1q25.3 MRI locus gives rise not only to the originally reported 1,263-bp cDNA *clone encoding a putative 341-amino acid polypeptide chain, but to many* additional transcripts in various tissues as well. Here we define the molecular identity of all human and murine MR1 isoforms generated through a complex scenario of *alternative splicing, some encoding secretory* variants lacking the Ig-like **alpha 3** domain, Moreover, we show ubiquitous transcription of these MR1 variants in several major cell lineages. We additionally report the complete 16,769-bp genomic structure off the MR1 locus, localize the murine orthologue to a syntenic segment of chromosome I, and provide evidence for conservation of a single-copy MRI gene throughout mammalian evolution. The 90% sequence identity between the human and mouse MRI putative ligand binding domains together with the ubiquitous expression of this gene favor broad immunobiologic relevance.

L6 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998225335 MEDLINE
DOCUMENT NUMBER: 98225335
TITLE: **Hemochromatosis** and iron needs.
AUTHOR: Halliday J W
CORPORATE SOURCE: Queensland Institute of Medical Research, Bancroft Centre,
Royal Brisbane Hospital, Queensland, Australia.
SOURCE: NUTRITION REVIEWS, (1998 Feb) 56 (2 Pt 2) s30-7; discussion
s54-75. Ref: 41
Journal code: OAY. ISSN: 0029-6643.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
ENTRY MONTH: 199807
ENTRY WEEK: 19980704
AB Although iron is an essential dietary requirement, the amount absorbed by the body is well regulated and depends on body iron stores and on dietary iron availability. There is very little iron excreted under normal conditions. Iron deficiency is a worldwide problem but iron overload, as seen in the inherited disease, **hemochromatosis**, is a major cause of morbidity in some Caucasian populations. This is a problem particularly *where there is an adequate dietary iron intake and especially in males. A* mutation has recently been described in an **MHC** Class I-like gene (HFE) that encodes for a protein (HFE) of 343 amino acids. The molecule *contains a signal sequence peptide-binding region, alpha, and alpha(2)* domains, and an immunoglobulinlike **alpha(3)** domain, in addition to a transmembrane region and a small cytoplasmic tail. It is a candidate gene for **hemochromatosis**. Several possibilities as to the function of this gene and the corresponding protein have been suggested but none has yet been confirmed. The mutation has been detected by several different groups in 80%-100% of subjects with the disease. However, in one study, 18%-20% of patients with the mutation did not exhibit significant iron overload. The discovery of this gene has important implications for both clinical studies and the elucidation of *the pathways of iron metabolism.*

L6 ANSWER 3 OF 3 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998128551 EMBASE
TITLE: **Hemochromatosis** and iron needs.
AUTHOR: Halliday J.W.
CORPORATE SOURCE: Dr. J.W. Halliday, QLD Institute of Medical Research, The
Bancroft Centre, PO Royal Brisbane Hospital, Brisbane, QLD 4029, Australia
SOURCE: Nutrition Reviews, (1998) 56/2 II (S30-S37).
Refs: 41
ISSN: 0029-6643 CODEN: NUREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB *Although iron is an essential dietary requirement,* the amount absorbed by the body is well regulated and depends on body iron stores and on dietary iron availability There is very little iron excreted under normal conditions. Iron deficiency is a worldwide problem but iron overload, as seen in the inherited disease, **hemochromatosis**, is a major cause of morbidity in some Caucasian populations. This is a problem particularly where there is an adequate dietary iron intake and especially in males. A mutation has recently been described in an **MHC** Class I-like gene (HFE) that encodes for a protein (HFE) of 343 amino acids. The molecule contains a signal sequence peptide-binding region, .alpha.1 and .alpha.2 domains, and an immunoglobulin-like .**alpha.3** domain, *in addition to a transmembrane region* and a small cytoplasmic tail. It is a candidate gene for **hemochromatosis**. Several possibilities as to the function of this gene and the corresponding protein have been suggested but none has yet been confirmed. *The mutation has been* detected by several different groups in 80%-100% of subjects with the disease. However, in one study, 18%-20% of patients with the mutation did not exhibit significant iron overload. The discovery of this gene has important implications for both clinical studies and the elucidation of the pathways of iron metabolism.

=> s l2 and alpha-1

2 FILES SEARCHED...
5 FILES SEARCHED...
L7 4 L2 AND ALPHA-1

=> dup rem

ENTER L# LIST OR (END):l7

PROCESSING COMPLETED FOR L7
L8 4 DUP REM L7 (0 DUPLICATES REMOVED)

=> d l8 1-4 ibib ab

L8 ANSWER 1 OF 4 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 1998:793658 SCISEARCH
THE GENUINE ARTICLE: 127TU
TITLE: Expanded genomic organization of conserved mammalian **MHC** class *I-related genes, human MR1 and its* murine ortholog
AUTHOR: Yamaguchi H; Kurosawa Y; Hashimoto K (Reprint)
CORPORATE SOURCE: FUJITA HLTH UNIV, INST *COMPREHENS MED SCI,* TOYOAKE, AICHI
47011, JAPAN (Reprint); FUJITA HLTH UNIV, INST COMPREHENS
MED SCI, TOYOAKE, AICHI 47011, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (29
SEP 1998) Vol. 250, No. 3, pp. 558-564.
Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525
B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0006-291X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 52
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB MR1 is a major histocompatibility complex (**MHC**) class *I-related gene located outside the human* **MHC**. Among several divergent class I molecules, the predicted MR1 molecule is closest, in the alpha 1 and alpha 2 domains, to the class I group to which the vertebrate *classical class I molecules belong. We report here* the genomic organizations of the human MR1 and mouse MR1 genes. Both genes exhibit genomic structures largely similar to those of the **MHC** class I genes. However, they are highly expanded in their scale in contrast to the classical **MHC** class I genes. Inclusion of transposable elements into introns seems to partly contribute to these genomic structures. Several other **MHC** class I-related genes also

show relatively large genomic structures. The present study extended heterogeneity in the genomic organization among the class I gene family by revealing a highly expanded structure of the human MR1 gene and its murine ortholog. (C) 1998 Academic Press.

L8 ANSWER 2 OF 4 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 1998:284519 SCISEARCH
THE GENUINE ARTICLE: ZF840
TITLE: **Hemochromatosis** and iron needs
AUTHOR: Halliday J W (Reprint)
CORPORATE SOURCE: ROYAL BRISBANE HOSP, BANCROFT CTR, QUEENSLAND INST MED
RES, BRISBANE, QLD 4029, AUSTRALIA (Reprint)
COUNTRY OF AUTHOR: AUSTRALIA
SOURCE: NUTRITION REVIEWS, (FEB 1998) Vol. 56, No. 2, Part 2, pp. S30-S37.
Publisher: INT LIFE SCIENCES INST, 810 EAST 10TH ST SUBSCRIPTION OFFICE, LAWRENCE, KS 66044.
ISSN: 0029-6643.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE; AGRI
LANGUAGE: English
REFERENCE COUNT: 41
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
Although iron is an essential dietary requirement, the amount absorbed by the body is well regulated and depends on body iron stores and on dietary iron availability. There is very little iron excreted under normal conditions. Iron deficiency is a worldwide problem but iron overload, as seen in the inherited disease, **hemochromatosis**, is a major cause of morbidity in some Caucasian populations. This is a problem particularly where there is an adequate dietary iron intake and especially in males. A mutation has recently been described in an **MHC** Class I-like gene (HFE) that encodes for a protein (HFE) of 343 amino acids. The molecule contains a signal sequence peptide-binding region, **alpha**(1) and alpha(2) domains, and an immunoglobulinlike alpha(3) domain, in addition to a transmembrane region and a small cytoplasmic tail. It is a candidate gene for **hemochromatosis**. Several possibilities as to the function of this gene and the corresponding protein have been suggested but none has yet been confirmed. The mutation has been defected by several different groups in 80%-100% of subjects with the disease. However, in one study, 18%-20% of patients with the mutation did not exhibit significant iron overload. The discovery of this gene has important implications for both clinical studies and the elucidation of the pathways of iron metabolism.

L8 ANSWER 3 OF 4 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998128551 EMBASE
TITLE: **Hemochromatosis** and iron needs.
AUTHOR: Halliday J.W.
CORPORATE SOURCE: Dr. J.W. Halliday, QLD Institute of Medical Research, The
Bancroft Centre, PO Royal Brisbane Hospital, Brisbane, QLD 4029, Australia
SOURCE: Nutrition Reviews, (1998) 56/2 II (S30-S37).
Refs: 41
ISSN: 0029-6643 CODEN: NUREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although iron is an essential dietary requirement, the amount absorbed by the body is well regulated and depends on body iron stores and on dietary iron availability There is very little iron excreted under normal conditions. Iron deficiency is a worldwide problem but iron overload, as seen in the inherited disease, **hemochromatosis**, is a major cause of morbidity in some Caucasian populations. This is a problem particularly where there is an adequate dietary iron intake and especially in males. A mutation has recently been described in an **MHC** Class I-like gene (HFE) that encodes for a protein (HFE) of 343 amino acids. The molecule contains a signal sequence peptide-binding region, .**alpha**. 1 and .alpha.2 domains, and an immunoglobulin-like .alpha.3 domain, in addition to a transmembrane region and a small cytoplasmic tail. It is a candidate gene for **hemochromatosis**. Several possibilities as to the function of this gene and the corresponding protein have been suggested but none has yet been confirmed. The mutation has been detected by several different groups in 80%-100% of subjects with the disease. However, in one study, 18%-20% of patients with the mutation did not exhibit significant iron overload. The discovery of this gene has important implications for both clinical studies and the elucidation of the pathways of iron metabolism.

L8 ANSWER 4 OF 4 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97149609 EMBASE
TITLE: Identification of a mouse homolog for the human hereditary haemochromatosis candidate gene.
AUTHOR: Hashimoto K.; Hirai M.; Kurosawa Y.
CORPORATE SOURCE: Japan. keihashi@fujita-hu.ac.jp.
SOURCE: Biochemical and Biophysical Research Communications, (1997)
230/1 (35-39).
Refs: 17
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recently, a novel human major histocompatibility complex (**MHC**) class I-like gene (HLA-H) was reported as a candidate gene for human hereditary haemochromatosis, a recessive disease of iron metabolism with a remarkably high incidence in northern Europeans. Independently we have isolated this gene in the course of a search for new human **MHC** class I-related genes and named it MR2. Here we report a mouse homolog of this human gene. The mouse MR2 gene is similar to the human counterpart with an overall predicted amino acid sequence similarity of .apprx. 66% and it is expressed in various tissues as in human. The extra eight amino acid residues between the .**alpha.1** and the .alpha.2 domains in the mouse molecule compared to the human counterpart can be explained by the creation of the coding sequence from the intron. While the human gene is located at the site telomeric to the **MHC** region on human chromosome 6, our study indicated the translocation of the mouse homolog from the site telomeric to the **MHC** on mouse chromosome 17 to chromosome 13 along with other genes. This mouse gene should be important in clarifying a possible role in iron metabolism.

=> s l1 and mhc and class-1

4 FILES SEARCHED...
L9 36 L1 AND MHC AND CLASS-1

=> dup rem

ENTER L# LIST OR (END):l9

PROCESSING COMPLETED FOR L9
L10 29 DUP REM L9 (7 DUPLICATES REMOVED)

=> d l10 1-29 ibib ab

L10 ANSWER 1 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998166454 EMBASE
TITLE: Adaptive response of iron absorption to anemia, increased erythropoiesis, iron deficiency, and iron loading in .beta.2-microglobulin knockout mice.
AUTHOR: Santos M.; Clevers H.; De Sousa M.; Marx J.J.M.
CORPORATE SOURCE: M. Santos, Department of Immunology, University Hospital
Utrecht, Heidelberglaan 100, 3584 CX Utrecht, Netherlands
SOURCE: Blood, (15 Apr 1998) 91/8 (3059-3065).
Refs: 36
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recently, a novel gene of the major histocompatibility complex (**MHC**) class I family, HFE (HLA-H), has been found to be mutated in a large proportion of hereditary **hemochromatosis** (HH) patients. Further support for a causative role of HFE in this disease comes from the observation that .beta.2- microglobulin knockout (.beta.2m(-/-)) mice, that fail to express **MHC** class I products, develop iron overload. We have now used this animal model of HH to examine the capacity to adapt iron absorption in response to altered iron metabolism in the absence of .beta.2m-dependent molecule(s). Mucosal uptake, mucosal transfer and retention of iron were measured in control and .beta.2m(-/-) mice with altered iron metabolism. Mucosal uptake of Fe(III), but not of Fe(II), by the mutant mice was significantly higher when compared with B6 control mice. Mucosal transfer in the .beta.2m(-/-) mice was higher, independent of the iron form tested. No significant differences were found in iron absorption between control and .beta.2m(-/-) mice when anemia was induced either by repetitive bleeding or by hemolysis through phenylhydrazine treatment. However, iron absorption in mice made anemic by dietary deprivation of iron was significantly higher in the mutant mice. Furthermore, the .beta.2m(-/-) mice manifested an impaired capacity to downmodulate iron absorption when dietary or parenterally iron-loaded. The expression of the defect in iron absorption in the .beta.2m(-/-) mice is quantitative, with iron absorption being excessively high for the size of body iron stores. The higher iron absorption capacity in the .beta.2m(-/-) mice may involve the initial stop of ferric mucosal uptake and the subsequent step of mucosal transfer of iron to the plasma.

L10 ANSWER 2 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999009625 EMBASE
TITLE: Kupffer cell staining by an HFE-specific monoclonal antibody: Implications for hereditary haemochromatosis.
AUTHOR: Bastin J.M.; Jones M.; O'Callaghan C.A.; Schimanski L.; Mason D.Y.; Townsend A.R.M.
CORPORATE SOURCE: Dr. J.M. Bastin, Department of Molecular Immunology,
Institute of Molecular Medicine, John Radcliffe Hospital, Oxford OX3 9DS, United Kingdom
SOURCE: British Journal of Haematology, (1998) 103/4 (931-941).
Refs: 41
ISSN: 0007-1048 CODEN: BJHEAL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
025 Hematology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hereditary haemochromatosis is an inherited disorder of iron absorption that leads to excessive iron storage in the liver and other organs. A candidate disease gene HFE has been identified that encodes a novel **MHC** class I like protein. We report the development of a monoclonal antibody (HFE-JB1) specific for recombinant refolded HFE protein. The antibody immunoprecipitates a 49 kD protein from the cell line U937, a histiocytic lymphoma. It binds HFE but does not recognize other recombinant non-classic **MHC** class I proteins (HLA-E, F and G), nor does it react with a variety of recombinant classic class I **MHC** molecules. COS cells transfected with HFE in culture are stained specifically. The immunohistochemical staining pattern in human tissues is unique and can be defined as a subset of the transferrin receptor positive cells. In the liver HFE protein was shown to be present on Kupffer cells and endothelium (sinusoidal lining cells), but absent from the parenchyma. Kupffer cells from an untreated C282Y HH patient failed to stain with the antibody. In the normal gut scattered cells in the crypts are stained, HFE was also present on capillary endothelium in the brain (a site of high levels of transferrin receptor) and on scattered cells in the cerebellum and cortex. These results raise interesting questions concerning the function of HFE in the control of body iron content and distribution.

L10 ANSWER 3 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998321190 EMBASE
TITLE: Hereditary juvenile haemochromatosis: A genetically heterogeneous life-threatening iron-storage disease.
AUTHOR: Kelly A.L.; Rhodes D.A.; Roland J.M.; Schofield P.; Cox T.M.
CORPORATE SOURCE: Prof. T.M. Cox, Department of Medicine, University of Cambridge, Addenbrooke's Hospital, Cambridge CB2 2QQ, United Kingdom

SOURCE: QJM - Monthly Journal of the Association of Physicians, (1998) 91/9 (607-618).
Refs: 48
ISSN: 0033-5622 CODEN: QMJPFH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Juvenile haemochromatosis is a rare inborn error of iron metabolism with clinical manifestations before 30 years of age. Unlike adult haemochromatosis which principally affects men, juvenile haemochromatosis affects the sexes equally; it causes early endocrine failure, dilated cardiomyopathy and joint disease. We report four patients (two of each sex) from three pedigrees affected by juvenile haemochromatosis with a mean onset at 22 years (range 14-30). All had endocrine deficiency with postpubertal gonadal failure secondary to pituitary disease; two suffered near-fatal cardiomyopathy with heart failure. Mean time to diagnosis from the first clinical signs of disease was 9.8 years (range 0.5-20) but general health and parameters of iron storage responded favourably to iron-depletion therapy. A 24-year-old man listed for heart transplantation because of cardiomyopathy [left ventricular (LV) ejection fraction 16%] responded to intravenous iron chelation with desferrioxamine combined with phlebotomy (ejection fraction 31%). A 27-year-old woman with subacute biventricular heart failure refractory to medication required orthotopic cardiac transplantation before the diagnosis was established (LV ejection fraction 25%). Genetic studies showed that these two patients with cardiomyopathy from unrelated families were heterozygous for the HFE 845G.fwdarw.A (C282Y) mutation and wild-type at the H63D locus: complete sequencing of the intron-exon boundaries and entire coding sequence of the HFE gene failed to identify additional lesions. Two siblings in a pedigree without cardiomyopathy were wild-type at the HFE C282Y locus; although the brother harboured a single copy of the 187C.fwdarw.G (H63D) allele, segregation analysis showed that in neither sibling was the iron-storage disease linked to MHC Class I markers on chromosome 6p. Juvenile haemochromatosis is thus a genetically heterogenous disorder distinct from the common adult variant.

L10 ANSWER 4 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998358355 EMBASE
TITLE: Cloning of a new gene (FB19) within HLA class I region.
AUTHOR: Totaro A.; Grifa A.; Carella M.; Rommens J.M.; Valentino M.A.; Roetto A.; Zelante L.; Gasparini P.
CORPORATE SOURCE: J.M. Rommens, Department of Genetics, Research Institute, The Hospital for Sick Children, Toronto, Canada
SOURCE: Biochemical and Biophysical Research Communications, (29 Sep 1998) 250/3 (555-557).
Refs: 4
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A novel gene (named FB19) has been identified within the HLA class I region at human chromosome 6p21.3. A 4.5-kb cDNA containing a 2820-bp open reading frame for a predicted protein of 940 aa was identified. No homology with known gene was detected at the DNA level, while the predicted protein is characterized by a glycine-rich region followed by a domain of 35 residues that shows high homology with the CAT56 gene, another gene of MHC class I. A 4.5-kb transcript was detected in several tissues and cell lines, clearly indicating a wide distribution of expression. Once its function is defined, it could be possible to investigate the relationship between the FB19 gene and the several diseases already mapped within the HLA class I region.

L10 ANSWER 5 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999017988 EMBASE
TITLE: Interaction of the **hemochromatosis** gene product HFE with transferrin receptor modulates cellular iron metabolism.
AUTHOR: Eisenstein R.S.
CORPORATE SOURCE: Dr. R.S. Eisenstein, Department of Nutritional Sciences, University of Wisconsin-Madison, Madison, WI 53706, United States
SOURCE: Nutrition Reviews, (1998) 56/12 (356-358).
Refs: 15
ISSN: 0029-6643 CODEN: NUREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
022 Human Genetics
025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mutations of a novel MHC class I-like protein, termed HFE, have been found in the vast majority of patients with the iron overload disease heredity **hemochromatosis**. Identification of HFE is likely to shed light on one of the major enigmas of mammalian iron homeostasis: How is intestinal iron absorption regulated?.

L10 ANSWER 6 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998079801 EMBASE
TITLE: HFE codon 63/282 (H63D/C282Y) dimorphism in German patients with genetic **hemochromatosis**.
AUTHOR: Gottschalk R.; Seidl C.; Loffler T.; Seifried E.; Hoelzer D.; Kaltwasser J.P.
CORPORATE SOURCE: Dr. R. Gottschalk, Medizinische Klinik III, J.W. Goethe-Universitat, Theodor-Stern-Kai 7, D-60596 Frankfurt, Germany
SOURCE: Tissue Antigens, (1998) 51/3 (270-275).
Refs: 49
ISSN: 0001-2815 CODEN: TSANA2
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Genetic **hemochromatosis** (GH) is closely associated with genes of the major histocompatibility complex (MHC) on chromosome 6. Recently, a candidate gene for GH, with structural similarities to MHC class I genes, designated HLA-H and presently named HFE, has been cloned. The HFE gene is localized telomeric to the MHC and several reports have indicated that the HFE gene is mutated in GH patients. In the present study we have analyzed the relationship of HFE gene variants and disease manifestation in GH patients and family members. Fifty-seven patients with GH, 73 family members and 153 healthy blood donors were studied for the amino acid dimorphism at codon 63 (His63Asp = H63D) and codon 282 (Cys282Tyr = C282Y) of the HFE gene. The codon 63 and 282 dimorphism were defined by PCR amplification of genomic DNA samples and restriction enzyme digestion using RsaI/SnaBI for C282Y and BclI/MboI for H63D. Ferritin, transferrin serum levels and total iron-binding capacity were determined prior to therapeutic intervention. The Tyr-282 substitution occurred in 53 (93%) of patients compared with 8 (5.2%) of controls (OR = 169, P < 0.0001). Fifty-one (90%) patients were Tyr-282 homozygous. In contrast, the Asp-63 substitution was present in 5 (8.8%) of the patients compared with 34 (22%) of controls (OR = 0.39, P = NS) with none of the patients being homozygous. In Tyr-282 homozygous GH patients serum ferritin levels, transferrin saturation, liver iron and liver iron index were elevated significantly compared to Tyr-282-negative patients, whereas no difference was observed between Tyr/Cys-282 heterozygous and Tyr-282-negative patients.

L10 ANSWER 7 OF 29 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998181475 MEDLINE
DOCUMENT NUMBER: 98181475
TITLE: Relation of HFE gene mutations, high iron stores and early onset coronary artery disease.
AUTHOR: Nassar B A; Zayed E M; Title L M; O'Neill B J; Bata I R; Kirkland S A; Dunn J; Dempsey G I; Tan M H; Johnstone D E
CORPORATE SOURCE: Department of Pathology, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia.. nassar@is.dal.ca
SOURCE: CANADIAN JOURNAL OF CARDIOLOGY, (1998 Feb) 14 (2) 215-20.
Ref: 44
Journal code: CHP. ISSN: 0828-282X.
PUB. COUNTRY: Canada
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY WEEK: 19980602
AB OBJECTIVE: To determine the impact of mutations in the HFE gene (human leukocyte antigen H) on predisposition to coronary artery disease (CAD) in patients not diagnosed with hereditary **hemochromatosis**. BACKGROUND: Elevated iron stores can predispose to acute myocardial infarction. Two mutations (C282Y and H63D) in the novel major histocompatibility complex (MHC) class 1 gene HFE were found in most patients with hereditary **hemochromatosis** causing high iron stores. The effect of these mutations on predisposition to CAD has not been investigated previously. METHODS: Three hundred patients with a history of myocardial infarction or angina pectoris and angiographically documented CAD were studied. Patients were divided into two groups: group 1 (150 patients), manifesting early onset CAD and presenting with these findings under age 50 years; and group 2 (150 patients), presenting for the first time over age 65 years. Prevalence of the C282Y and H63D mutations was assessed by molecular analysis, and plasma ferritin was measured immunochemically. RESULTS: There was no difference in the prevalence of homozygous, heterozygous or compound heterozygous (C282Y/H63D) states between the groups. Males in group 1 had higher plasma ferritin than those in group 2 (234 +/- 174 micrograms/L versus 136 +/- 103 micrograms/L, P < 0.0001), but this was not significantly different in females (75 +/- 54 micrograms/L versus 92 +/- 73 micrograms/L, P = 0.26). Ferritin remained higher in group 1 than in group 2 males after exclusion of mutation carriers (195 +/- 121 micrograms/L versus 109 +/- 76 micrograms/L, respectively, P < 0.0001), but did not change in females. CONCLUSIONS: Higher iron stores were found in males with early onset CAD. This association was not related to the C282Y or H63D mutation in HFE. It is suggested that association of the MHC locus with delayed onset CAD is probably unrelated to HFE in these patients, and that HFE mutations are not a major risk factor in the development of high iron stores in early onset CAD.

L10 ANSWER 8 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998383165 EMBASE
TITLE: [Pathogenesis, clinical manifestations and therapy of **hemochromatosis**, one of the most frequent hereditary diseases]. HAMOCHROMATOSE - PATHOGENESE, KLINIK UND THERAPIE EINER DER HAUFIGSTEN ERBKRANKHEITEN.
AUTHOR: Herrmann T.; Riedel H.D.; Gehrke S.G.; Stremmel W.
CORPORATE SOURCE: Dr. T. Herrmann, Abteilung Innere Medizin IV, Medizinische Klinik und Poliklinik, Klin. der Rupercht-Karls-Universitat, Bergheimer Strasse 58, D-69115 Heidelberg, Germany
SOURCE: Verdauungskrankheiten, (1998) 16/5 (214-222).
Refs: 30
ISSN: 0174-738X CODEN: VERDEJ
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB **Hemochromatosis** represents the most frequent autosomal recessively inherited disease, with an estimated frequency between 1 in 400 and 1 in 200 individuals. The genetic defect is localized on

chromosome 6 close to the HLA-A locus and has recently been characterized as a mutation in a **MHC** class I gene, originally named HLA-H and subsequently designated HFE. Pathophysiologically, an increase in intestinal iron absorption is observed. Iron accumulation principally affects liver, pancreas, heart, gonadotropic cells of the pituitary gland, skin and joints. Liver cirrhosis, cardiomyopathy, diabetes mellitus, hypogonadism, skin pigmentation, and arthropathy are frequent manifestations. Elevation of serum ferritin level and high serum transferrin saturation are typical laboratory findings. In men, full phenotypic expression occurs about 10 times more frequently than in women.

First symptoms can be observed at the age of 20 to 40 years in men and after menopause in women, respectively. Adequate therapy consists in repeated phlebotomies. Desferoxamine therapy should be restricted to patients with secondary iron overload and anemia in whom phlebotomies are not feasible. Early diagnosis and therapy largely prevent the adverse consequences of iron overload.

L10 ANSWER 9 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998307551 EMBASE
TITLE: Haemochromatosis.
AUTHOR: Crawford D.H.G.; Leggett B.A.; Powell L.W.
CORPORATE SOURCE: Dr. L.W. Powell, Queensland Institute of Medical [illegible]., The Bancroft Centre, Brisbane, QLD, Australia
SOURCE: Bailliere's Clinical Gastroenterology, (1998) 12/2 (209-225).
Refs: 70
ISSN: 0950-3528 CODEN: BCGAER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Primary, hereditary or genetic haemochromatosis is one of the most common inherited disorders in a Caucasian populations with a disease frequency of 1:300-400 and a carrier frequency of approximately 10%. The basic genetic defect remains unknown, although the haemochromatosis gene has now been cloned and is known to be a member of the **MHC** non-classical class I family. Many factors - environmental, genetic and non-genetic in nature - influence the degree of iron loading in affected individuals. In particular, pathological and physiological blood loss influence iron stores in haemochromatosis. The iron concentration in the liver is an important determinant of survival because a hepatic iron concentration in excess of 400 .mu.mol/g dry weight is usually associated with cirrhosis. Patients with cirrhosis secondary to haemochromatosis are at risk of hepatocellular carcinoma. The combination of improved awareness of the disease and the appropriate use of genetic testing for the common C282Y mutation should lead to earlier diagnosis and therapy.

L10 ANSWER 10 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97376727 EMBASE
DOCUMENT NUMBER: 1997376727
TITLE: Association of the transferrin receptor in human placenta with HFE, the protein defective in hereditary **hemochromatosis**.
AUTHOR: Parkkila S.; Waheed A.; Britton R.S.; Bacon B.R.; Zhou X.Y.; Tomatsu S.; Fleming R.E.; Sly W.S.
CORPORATE SOURCE: W.S. Sly, E.A. Doisy Biochem./Mol. Biol. Dept., Saint Louis Univ. School of Medicine, 1402 South Grand Boulevard, St. Louis, MO 63104, United States. slyws@wpogate.slu.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) 94/24 (13198-13202).
Refs: 27
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hereditary **hemochromatosis** (HH) is a common autosomal recessive disease associated with loss of regulation of dietary iron absorption and excessive iron deposition in major organs of the body. Recently, a candidate gene for HH (also called HFE) was identified that encodes a novel **MHC** class I-like protein. Most patients with HH are homozygous for the same mutation in the HFE gene, resulting in a C282Y change in the HFE protein. Studies in cultured cells show that the C282Y mutation abrogates the binding of the recombinant HFE protein to .beta.2-microglobulin (.beta.2M) and disrupts its transport to the cell surface. The HFE protein was shown by immunohistochemistry to be expressed in certain epithelial cells throughout the human alimentary tract and to have a unique localization in the cryptal cells of small intestine, where signals to regulate iron absorption are received from the body. In the studies presented here, we demonstrate by immunohistochemistry that the HFE protein is expressed in human placenta in the apical plasma membrane of the syncytiotrophoblasts, where the transferrin-bound iron is normally transported to the fetus via receptor-mediated endocytosis. Western blot analyses show that the HFE protein is associated with .beta.2M in placental membranes. Unexpectedly, the transferrin receptor was also found to be associated with the HFE protein/.beta.2M complex. These studies place the normal HFE protein at the site of contact with the maternal circulation where its association with transferrin receptor raises the possibility that the HFE protein plays some role in determining maternal/fetal iron homeostasis. These findings also raise the question of whether mutations in the HFE gene can disrupt this association and thereby contribute to some forms of neonatal iron overload.

L10 ANSWER 11 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97183449 EMBASE
TITLE: Haplotype analysis of **hemochromatosis**: Evaluation of different linkage- disequilibrium approaches and evolution of disease chromosomes.
AUTHOR: Ajioka R.S.; Jorde L.B.; Gruen J.R.; Yu P.; Dimitrova D.; Barrow J.; Radisky E.; Edwards C.Q.; Griffen L.M.; Kushner J.P.
CORPORATE SOURCE: Dr. R.S. Ajioka, Division of Hematology/Oncology, Univ. of Utah Health Sciences Center, 50 North Medical Drive, Salt Lake City, UT 84132, United States
SOURCE: American Journal of Human Genetics, (1997) 60/6 (1439-1447).
Refs: 49
ISSN: 0002-9297 CODEN: AJHGAG
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We applied several types of linkage-disequilibrium calculations to analyze the hereditary **hemochromatosis** (hh) locus. Twenty-four polymorphic markers in the major histocompatibility complex (**MHC**) class I region were used to haplotype hh and normal chromosomes. A total of 169 hh and 161 normal chromosomes were analyzed. Disequilibrium values were found to be high over an unusually large region beginning 150 kb centromeric of HLA-A and extending nearly 5 Mb telomeric of it. Recombination in this region was .apprx.28% of the expected value. This low level of recombination contributes to the unusually broad region of linkage disequilibrium found with hh. The strongest disequilibrium was found at locus HLA-H (.delta. = .84) and at locus D6S2239 (.delta. = .85), a marker .apprx.10 kb telomeric to HLA-H. All disequilibrium methods employed in this study found peak disequilibrium at HLA-H or D6S2239. The cys282tyr mutation in HLA-H, a candidate gene for hh, was found in 85% of disease chromosomes. A haplotype phylogeny for hh chromosomes was constructed and suggests that the mutation associated with the most common haplotype occurred relatively recently. The age of the hh mutation was estimated to be .apprx.60-70 generations. Disequilibrium was maintained over a greater distance for hh-carrying chromosomes, consistent with a recent mutation for hh. Our data provide a reasonable explanation for previous difficulties in localizing the hh locus and provide an evolutionary history for disease chromosomes.

L10 ANSWER 12 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998042880 EMBASE
TITLE: A 1200-kilobase transcription map encompassing the D6S105 locus at 6p21.3.
AUTHOR: Mosser J.; Andrieux N.; Fergelot P.; Gicquel I.; Lelaure V.; Galibert F.; David V.
CORPORATE SOURCE: J. Mosser, UPR 41 CNRS 'Recombinaisons Genet.', Faculte de Medecine, 2 avenue du Professeur Leon Bernard, 35043 Rennes Cedex, France. mosser@univrennes1.fr
SOURCE: Genomics, (1997) 46/3 (487-490).
Refs: 12
ISSN: 0888-7543 CODEN: GNMCEP
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The gene content of the **MHC** class I telomerically adjacent region, in linkage disequilibrium with hereditary **hemochromatosis**, has not been well characterized yet. In the present work, we established three bacterial clone contigs, including mainly P1-derived artificial chromosomes. These contigs cover 89% of the 1.2-Mb 6p-subtelomeric region encompassing locus D6S105. Terminal exon trapping was applied to selected clones from these contigs. Forty-six independent terminal exons were identified and mapped within the region, 2 of which matched perfectly to expressed sequence tags. These 3' exons are all expressed in human fetal brain but differentially expressed in four tissues and two cell lines. The high number of exons identified indicates that the high gene density observed in the **MHC** class I region extends to this telomerically adjacent region.

L10 ANSWER 13 OF 29 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97294057 MEDLINE
DOCUMENT NUMBER: 97294057
TITLE: A 1.1-Mb transcript map of the hereditary **hemochromatosis** locus.
AUTHOR: Ruddy D A; Kronmal G S; Lee V K; Mintier G A; Quintana L; Domingo R Jr; Meyer N C; Irrinki A; McClelland E E; Fullan A; Mapa F A; Moore T; Thomas W; Loeb D B; Harmon C; Tsuchihashi Z; Wolff R K; Schatzman R C; Feder J N
CORPORATE SOURCE: Mercator Genetics, Menlo Park, California 94025, USA.
SOURCE: GENOME RESEARCH, (1997 May) 7 (5) 441-56.
Journal code: CES. ISSN: 1088-9051.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U90543; GENBANK-U90544; GENBANK-U90545; GENBANK-U90546; GENBANK-U90547; GENBANK-U90548; GENBANK-U90550; GENBANK-U90551; GENBANK-U90552; GENBANK-U91328; GENBANK-U60319
ENTRY MONTH: 199710
ENTRY WEEK: 19971002
AB In the process of positionally cloning a candidate gene responsible for hereditary **hemochromatosis** (HH), we constructed a 1.1-Mb transcript map of the region of human chromosome 6p that lies 4.5 Mb telomeric to HLA-A. A combination of three gene-finding techniques, direct cDNA selection, exon trapping, and sample sequencing, were used initially for a saturation screening of the 1.1-Mb region for expressed sequence fragments. As genetic analysis further narrowed the HH candidate locus, we sequenced completely 0.25 Mb of genomic DNA as a final measure to identify all genes. Besides the novel **MHC class 1** -like HH candidate gene HLA-H, we identified a family of five butyrophilin-related sequences, two genes with structural similarity to a type 1 sodium phosphate transporter, 12 novel histone genes, and a gene we named RoRet based on its strong similarity to the 52-kD Ro/SSA lupus and Sjogren's syndrome auto-antigen and the RET finger protein. Several members of the butyrophilin family and the RoRet gene share an exon of common evolutionary origin called B30-2. The B30-2 exon was originally isolated from the HLA **class 1** region, yet has apparently "shuffled" into several genes along the chromosome telomeric to the **MHC**. The conservation of the B30-2 exon in several novel genes and the previously described amino acid homology of HLA-H to

MHC class 1 molecules provide further support
that this gene-rich region of 6p21.3 is related to the MHC.
Finally, we performed an analysis of the four approaches for gene finding
and conclude that direct selection provides the most effective probes for
cDNA screening, and that as much as 30% of ESTs in this 1.1-Mb region
may
be derived from noncoding genomic DNA.

L10 ANSWER 14 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97071931 EMBASE
TITLE: The MHC contains multiple genes potentially
relevant to hemochromatosis.
AUTHOR: Tay G.K.; Leelayuwat C.; Chorney M.J.; Cattley S.K.;
Hollingsworth P.N.; Witt C.S.; Daly L.N.; Hughes A.;
Dawkins R.L.
CORPORATE SOURCE: Australia
SOURCE: Immunogenetics, (1997) 45/5 (336-340).
Refs: 32
ISSN: 0093-7711 CODEN: IMNGBK
COUNTRY: Germany, Federal Republic of
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
NGUAGE: English

L10 ANSWER 15 OF 29 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 3
ACCESSION NUMBER: 1997:110532 BIOSIS
DOCUMENT NUMBER: PREV199799409735
TITLE: Increased frequency of the haemochromatosis Cys282Tyr
mutation in sporadic porphyria cutanea tarda.
AUTHOR(S): Roberts, Andrew G.; Whatley, Sharon D.; Morgan, Rhian R.;
Worwood, Mark; Elder, George H. (1)
CORPORATE SOURCE: (1) Dep. Med. Biochem., Univ. Wales Coll. Med.,
Health
Park, Cardiff CF4 4XN UK
SOURCE: Lancet (North American Edition), (1997) Vol. 349, No. 9048,
pp. 321-323.
ISSN: 0099-5355.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Background: Sporadic porphyria cutanea tarda is a skin disease associated
with hepatic siderosis. Depletion of iron stores by phlebotomy is
curative. The role of hemochromatosis genes in determining
susceptibility to this disorder is controversial. We have examined the
frequency in sporadic porphyria cutanea tarda of mutations (Cys282Tyr,
His63Asp) in a novel MHC class-1-like gene,
one of which (Cys282Tyr) is believed to cause hemochromatosis.
Methods: 41 patients with sporadic porphyria cutanea tarda, in whom the
frequency of microsatellite alleles that define the ancestral
hemochromatosis haplotype had previously been determined, and 101
healthy blood donors were studied for the presence of the Cys282Tyr and
His63Asp mutations. We used restriction-enzyme digestion of PCR-amplified
genomic DNA. Findings: The Cys282Tyr mutation occurred in 18 (44%) of
patients compared with 11 (11%) of controls (relative risk 6.2, 95% CI
2.6-14.5, p = 0.00003). Seven (17%) patients, aged 48-79 years, were
homozygotes. In 12 patients, the Cys282Tyr mutation was associated with
markers of the HLA-A3-containing ancestral hemochromatosis
haplotype. Ages at presentation were the same for those with or without
the Cys282Tyr mutation. There was no difference in the frequency of the
His63Asp mutation. Interpretation: Inheritance of one or more
hemochromatosis genes is an important susceptibility factor for
sporadic porphyria cutanea tarda. Some homozygotes for the Cys282Tyr
mutation present late in life with porphyria cutanea tarda, indicating
that not all homozygotes present clinically with hemochromatosis
. The relation between this genotype and disease needs further
investigation.

L10 ANSWER 16 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97071929 EMBASE
TITLE: Mutations in the MHC class I-like candidate gene
for hemochromatosis in French patients.
AUTHOR: Borot N.; Roth M.-P.; Malfroy L.; Demangel C.; Vinel J.-P.;
Pascal J.-P.; Coppin H.
CORPORATE SOURCE: France
SOURCE: Immunogenetics, (1997) 45/5 (320-324).
Refs: 19
ISSN: 0093-7711 CODEN: IMNGBK
COUNTRY: Germany, Federal Republic of
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A candidate gene for hemochromatosis has recently been localized
on the short arm of chromosome 6, about 4 megabases telomeric to the
major
histocompatibility complex. It encodes a protein that exhibits significant
similarity to the HLA class I molecules and can be provisionally
designated HLA-hc. Genotype analysis of 94 hemochromatosis
patients living in France and a similar number of controls confirms that
the disease is strongly associated with homozygosity at nucleotide 845
(72% of the patients and none of the controls carry two copies of the 845A
variant). The data are consistent with hemochromatosis being a
heterogeneous disease: about 79% of the cases in this sample would be
caused by a defect in HLA-he and 21% by an unrelated mechanism. A
second
variant (187 G) enriched on patient chromosomes that do not carry the 845A
mutation might influence the affinity of a ligand for HLA-hc; the exact
nature of this ligand remains to be discovered. The 845A variant is the
best genetic marker for the disease identified to date, and the detection
of 845A homozygosity should now permit diagnosis of a readily curable
disease and the prevention of sometimes deadly complications in at least
72% of the patients.

L10 ANSWER 17 OF 29 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1997:539613 BIOSIS
DOCUMENT NUMBER: PREV199799838816
TITLE: Haemochromatosis mutations in North-East Scotland.
AUTHOR(S): Loughlin, Sam (1); Miedzybrodzka, Z. (1); Baty, D.; Terron,
A.; Kelly, K. (1); Dean, J. (1); Goudie, D.; Greaves, M.;
Haites, N. (1)
CORPORATE SOURCE: (1) Aberdeen Royal Hosp. NHS Trust, Dep. Med.
Genetics,
Med. Sch., Aberdeen AB25 2ZD UK
SOURCE: Journal of Medical Genetics, (1997) Vol. 34, No. SUPPL. 1,
pp. S80.
Meeting Info.: British Human Genetics Conference York,
England, UK September 15-17, 1997
ISSN: 0022-2593.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L10 ANSWER 18 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998015839 EMBASE
TITLE: Hereditary hemochromatosis: Recent advances in
molecular genetics and clinical management.
AUTHOR: Camaschella C.; Piperno A.
CORPORATE SOURCE: C. Camaschella, Dipto. Sci. Biomed./Oncologia
Umana,
Azienda Ospedaliera S. Luigi, 10043 Orbassano, Italy.
camaschella@csivms.csi.it
SOURCE: Haematologica, (1997) 82/1 (77-84).
Refs: 94
ISSN: 0390-6078 CODEN: HAEMAX
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background and Objective. Hereditary hemochromatosis (HC) is an
inborn error of iron metabolism leading to increased intestinal iron
absorption and progressive iron overload. There have been definite
advances in our knowledge of the pathogenesis and management of
idiopathic
hemochromatosis in recent years, which prompted us to review this
subject. Information sources. The material examined in the present review
includes articles and abstracts published in the journals covered by the
Science Citation Index.RTM. and Medline.RTM.. In addition, both authors
have been working in this field for several years and have contributed
twelve of the papers cited in the references. State of art and
Perspectives. The disease is a late onset autosomic recessive condition,
especially frequent in Caucasians. If unrecognized, severe clinical
symptoms develop in mid-life related to organ failure. Early diagnosis
prevents complications, since an intensive phlebotomy course removes
excess iron and offers patients a normal life expectancy. Transferrin
saturation is the first examination step, but liver biopsy is still
essential for diagnosis and prognosis of HC. The biochemical defect is
unknown. Positional cloning of the HC gene has led to the isolation of all
the candidate region on the short arm of chromosome 6, telomeric to HLA-A.
Recently a putative HC gene has been cloned from this region and found to
be mutated in a large proportion of patients. The gene, known as HLA-H, is
an atypical MHC class I gone. Although its biological function
remains unknown, HLA-H is the first strong HC candidate gone. Molecular
screening of patients and carriers is now possible in a significant
portion of cases, thereby permitting better control of the disease. If it
is unequivocally confirmed that the HLA-H gene is responsible for the
disease, understanding of its biological function will provide information
on the type and activity of the involved protein, revealing new insights
into iron uptake and metabolism in humans.

L10 ANSWER 19 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97149609 EMBASE
TITLE: Identification of a mouse homolog for the human hereditary
haemochromatosis candidate gene.
AUTHOR: Hashimoto K.; Hirai M.; Kurosawa Y.
CORPORATE SOURCE: Japan. keihashi@fujita-hu.ac.jp.
SOURCE: Biochemical and Biophysical Research Communications,
(1997)
230/1 (35-39).
Refs: 17
ISSN: 0006-291X CODEN: BBRCA
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recently, a novel human major histocompatibility complex (MHC)
class I-like gene (HLA-H) was reported as a candidate gene for human
hereditary haemochromatosis, a recessive disease of iron metabolism with a
remarkably high incidence in northern Europeans. Independently we have
isolated this gene in the course of a search for new human MHC
class I-related genes and named it MR2. Here we report a mouse homolog of
this human gene. The mouse MR2 gene is similar to the human counterpart
with an overall predicted amino acid sequence similarity of .apprx. 66%
and it is expressed in various tissues as in human. The extra eight amino
acid residues between the .alpha.1 and the .alpha.2 domains in the mouse
molecule compared to the human counterpart can be explained by the
creation of the coding sequence from the intron. While the human gene is
located at the site telomeric to the MHC region on human
chromosome 6, our study indicated the translocation of the mouse homolog
from the site telomeric to the MHC on mouse chromosome 17 to
chromosome 13 along with other genes. This mouse gene should be
important
in clarifying a possible role in iron metabolism.

L10 ANSWER 20 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96075295 EMBASE
TITLE: .beta.2 Knockout mice develop parenchymal iron overload: A
putative role for class I genes of the major
histocompatibility complex in iron metabolism.
AUTHOR: Rothenberg B.E.; Voland J.R.
CORPORATE SOURCE: Billups-Rothenberg, Inc., P.O. Box 977, Del Mar, CA
92014,
United States
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (1996) 93/4 (1529-1534).
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hemochromatosis (HC) is an inherited disorder of iron
absorption, mapping within the human major histocompatibility complex (
MHC). We have identified a multigene system in the murine

MHC that contains excellent candidates for the murine equivalent of the human HC locus and implicate nonclassical class I genes in the control of iron absorption. This gene system is characterized by multiple copies of two head-to-head genes encoded on opposite strands and driven by one common regulatory motif. This regulatory motif has a striking homology to the promoter region of the .beta.-globin gene, a gene obviously involved in iron metabolism and hence termed .beta.-globin analogous promoter (.beta.GAP). Upstream of the .beta.GAP sequence are nonclassical class I genes. At least one of these nonclassical class I genes, Q2, is expressed in the gastrointestinal tract, the primary site of iron absorption. Also expressed in the gastrointestinal tract and downstream of the .beta.GAP motif is a second set of putative genes, termed Hephaestus (HEPH). Based on these observations, we hypothesized that the genes that seem to be controlled by the .beta.GAP regulatory motifs would be responsible for the control of Fe absorption. As a test of this hypothesis, we predicted that mice which have altered expression of class I gene products, the .beta.2-microglobulin knockout mice, [.beta.2m(-/-)], would develop Fe overload. This prediction was confirmed, and these results indicate .beta.2m-associated proteins are involved in the control of intestinal Fe absorption.

L10 ANSWER 21 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96237404 EMBASE
TITLE: A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis.
AUTHOR: Feder J.N.; Gnirke A.; Thomas W.; Tsuchihashi Z.; Ruddy D.A.; Basava A.; Dormishian F.; Domingo R. Jr.; Ellis M.C.; Fullan A.; Hinton L.M.; Jones N.L.; Kimmel B.E.; Kronmal G.S.; Lauer P.; Lee V.K.; Loeb D.B.; Mapa F.A.; Wolff R.K.; et al.
CORPORATE SOURCE: Mercator Genetics, Inc., 4040 Campbell Avenue, Menlo Park, CA 94025, United States
SOURCE: Nature Genetics, (1996) 13/4 (399-408). ISSN: 1061-4036 CODEN: NGENEC
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hereditary haemochromatosis (HH), which affects some 1 in 400 and has an estimated carrier frequency of 1 in 10 individuals of Northern European descent, results in multi-organ dysfunction caused by increased iron deposition, and is treatable if detected early. Using linkage-disequilibrium and full haplotype analysis, we have identified a 250-kilobase region more than 3 megabases telomeric of the major histocompatibility complex (MHC) that is identical-by-descent in 85% of patient chromosomes. Within this region, we have identified a gene related to the MHC class I family, termed HLA-H, containing two missense alterations. One of these is predicted to inactivate this class of proteins and was found homozygous in 83% of 178 patients. A role of this gene in haemochromatosis is supported by the frequency and nature of the major mutation and prior studies implicating MHC class I-like proteins in iron metabolism.

L10 ANSWER 22 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96271650 EMBASE
TITLE: Cloning of a human homologue of the mouse Tctex-5 gene within the MHC class I region.
AUTHOR: Giffon T.; Lepourcelet M.; Pichon L.; Jezequel P.; Bouric P.; Carn G.; Pontarotti P.; Le Gall J.-Y.; David V.
CORPORATE SOURCE: Dept. Biochem. Molecular Biology, UPR 41 CNRS 'Recomb. genetiques', Faculte de Medecine, 2 avenue du Professeur Leon Bernard, 35043 Rennes cedex, France
SOURCE: Immunogenetics, (1996) 44/5 (331-339). ISSN: 0093-7711 CODEN: IMNGBK
COUNTRY: Germany, Federal Republic of
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Using a positional cloning strategy to identify the hemochromatosis gene (HFE), we isolated seven cDNAs by cDNA selection from a region of 400 kilobases (kb) located near the HLA-A and HLA-F loci. In this paper, we report the study of one of the corresponding genes, referred to as HCG V (hemochromatosis candidate gene), localized 150 kb centromeric to HLA-A. This gene was found to be expressed ubiquitously in the form of a 1.8 kb transcript, and to be apparently well conserved during evolution. The gene spanned 3.1 kb and is organized in three exons and two introns. The cDNA of 1620 base pairs (bp) showed an open reading frame of 378 bp, encoding for a 126 amino acid polypeptide which displayed a strong identity with the predicted product of a mouse Tctex-5 gene (t complex, testis expressed) localized in the t complex on chromosome 17. The HCG V gene was assessed as a potential candidate for hemochromatosis in regard to its localization in the linkage disequilibrium area between HFE and polymorphic markers. The study of deletions and point mutations in hemochromatosis patients revealed a single bp polymorphism within the coding region; however, no associated disease changes were found. Therefore we conclude that HCG V is unlikely to be involved in the pathogenesis of hemochromatosis.

L10 ANSWER 23 OF 29 MEDLINE
ACCESSION NUMBER: 97162703 MEDLINE
DOCUMENT NUMBER: 97162703
TITLE: Discovery of the hemochromatosis gene will require rethinking the regulation of iron metabolism.
AUTHOR: Fleet J C
CORPORATE SOURCE: Jean Mayer Human Nutrition Research Center on Aging, Tufts University, Boston MA 02111, USA.
SOURCE: NUTRITION REVIEWS, (1996 Sep) 54 (9) 285-7. Ref: 6
Journal code: OAY. ISSN: 0029-6643.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
ENTRY MONTH: 199704
ENTRY WEEK: 19970404
AB The identity of the protein responsible for hemochromatosis, the iron overload disease, has eluded scientists for years. However, a recent report identifies the gene where the hemochromatosis defect lies. It is a gene that encodes a major histocompatibility complex (MHC) class-1-like protein called HLA-H. The mechanism by which an HLA-H defect alters iron metabolism is still unidentified. However, this new discovery will certainly ignite a new wave of study into the physiology of iron metabolism and its regulation.

L10 ANSWER 24 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96244862 EMBASE
TITLE: A new non-HLA multigene family associated with the PERB11 family within the MHC class I region.
AUTHOR: Pichon L.; Hampe A.; Giffon T.; Carn G.; Legall J.Y.; David V.
CORPORATE SOURCE: Dept. Biochemistry Molecular Biology, UPR 41 CNRS Recombinaisons Genet., Faculte de Medecine, 2 avenue du Professeur Leon Bernard, 35043 Rennes Cedex, France
SOURCE: Immunogenetics, (1996) 44/4 (259-267). ISSN: 0093-7711 CODEN: IMNGBK
COUNTRY: Germany, Federal Republic of
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In an effort to initiate steps designed to characterize the idiopathic hemochromatosis disease gene, the HLA-A/HLA-F region where this gene is in disequilibrium linkage with some polymorphic markers has been overlapped by a yeast artificial chromosome (YAC) contig. In order to achieve the physical mapping of these YACs and of the corresponding genomic region, we subcloned one of the YACs involved. A computer-assisted analysis of the sequence of one subclone led to the isolation of a potential exon that proved to belong to a new expressed messenger named HCGIX. After Southern blot analysis, the corresponding cDNA clone was found to belong to a new multigene family whose members are dispersed throughout the HLA class I region and are closely associated with members of another recently described multigene family designated PERB11. The data reported here suggest that these two multigene families form a cluster that have been dispersed together throughout the telomeric part of the major histocompatibility complex and have been involved in the genesis of this human class I region.

L10 ANSWER 25 OF 29 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 96430000 MEDLINE
DOCUMENT NUMBER: 96430000
TITLE: Structural analysis of the HLA-A/HLA-F subregion: precise localization of two new multigene families closely associated with the HLA class I sequences.
AUTHOR: Pichon L; Carn G; Bouric P; Giffon T; Chauvel B; Lepourcelet M; Mosser J; Legall J Y; David V
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, CNRS, Recombinaisons genetiques, Rennes, France.
SOURCE: GENOMICS, (1996 Mar 1) 32 (2) 236-44. Journal code: GEN. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY WEEK: 19970705
AB Positional cloning strategies for the hemochromatosis gene have previously concentrated on a target area restricted to a maximum genomic expanse of 400 kb around the HLA-A and HLA-F loci. Recently, the candidate region has been extended to 2-3 Mb on the distal side of the MHC . In this study, 10 coding sequences [hemochromatosis candidate genes (HCG) I to X] were isolated by cDNA selection using YACs covering the HLA-A/HLA-F subregion. Two of these (HCG II and HCG IV) belong to multigene families, as well as other sequences already described in this region, i.e., P5, pMC 6.7, and HLA class 1. Fingerprinting of the four YACs overlapping the region was performed and allowed partial localization of the different multigene family sequences on each YAC without defining their exact positions. Fingerprinting on cosmids isolated from the ICRF chromosome 6-specific cosmid library allowed more precise localization of the redundant sequences in all of the multigene families and revealed their apparent organization in clusters. Further examination of these intertwined sequences demonstrated that this structural organization resulted from a succession of complex phenomena, including duplications and contractions. This study presents a precise description of the structural organization of the HLA-A/HLA-F region and a determination of the sequences involved in the megabase size polymorphism observed among the A3, A24, and A31 haplotypes.

L10 ANSWER 26 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96253817 EMBASE
TITLE: Structure and content of the major histocompatibility complex (MHC) class I regions of the great anthropoid apes.
AUTHOR: Venditti C.P.; Lawlor D.A.; Sharma P.; Chorney M.J.
CORPORATE SOURCE: Dept. of Microbiology and Immunology, Milton S. Hershey Medical Center, Pennsylvania State Univ. Med. Coll., Hershey, PA 17033, United States
SOURCE: Human Immunology, (1996) 49/2 (71-84). ISSN: 0198-8859 CODEN: HUIMDQ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The origins of the functional class I genes predated human speciation, a phenomenon known as trans-speciation. The retention of class Ia orthologues within the great apes, however, has not been paralleled by studies designed to examine the pseudogene content, organization, and structure of their class I regions. Therefore, we have begun the systematic characterization of the Old World primate MHCs. The numbers and sizes of fragments harboring class I sequences were similar among the chimpanzee, gorilla, and human genomes tested. Both of the gorillas included in our study possessed genomic fragments carrying

orthologues of the recently evolved HLA-H pseudogene identical to those found in the human. The overall megabase restriction fragment patterns of humans and chimpanzees appeared slightly more similar to each other, although the HLA-A subregional megabase variants may have been generated following the emergence of Homo sapiens. Based on the results of this initial study, it is difficult to generate a firm species tree and to determine human's closest evolutionary neighbor. Nevertheless, an analysis of **MHC** subregional similarities and differences in the hominoid apes may ultimately aid in localizing and identifying **MHC** haplotype-associated disease genes such as idiopathic **hemochromatosis**.

L10 ANSWER 27 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94261998 EMBASE
TITLE: Mapping and characterization of non-HLA multigene assemblages in the human **MHC** class I region.
AUTHOR: Venditti C.P.; Harris J.M.; Geraghty D.E.; Chorney M.J.
CORPORATE SOURCE: Department of Microbiology, Milton S. Hershey Medical Center, PSUCM, Hershey, PA 17033, United States
SOURCE: GENOMICS, (1994) 22/2 (257-266).
ISSN: 0888-7543 CODEN: GNMCEP
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
025 Hematology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The major histocompatibility complex (**MHC**) class I region has been shown to be associated with a variety of immune and nonimmune disorders. In an effort to initiate steps designed to identify the idiopathic **hemochromatosis** disease gene (HFE), we have cloned and mapped two expressed messages using probes from the HLA-H subregion that lie immediately distal to the HLA-A9 breakpoint. Although the cDNA clones identify distinct multifragment families that are dispersed throughout the **MHC**, the gene sequences from which the two cDNA clones derive map centromeric to the HLA-B locus and are absent from the genomes of higher nonhuman primates. This suggests that a syntenic coding segment arose within a highly polymorphic region (TNF to HLA-B interval) as the result of an insertion event following the emergence of Homo sapiens. An additional syntenic cluster exists within a peak of linkage disequilibrium with the HFE gene and may define coding sequences that underlie the defect in genetic iron overload. These data generally support the concept that the class I region is potentially gene-rich and further highlight the possibility that these new coding sequences may play a role in the development of a variety of HLA-linked diseases. The observations presented suggest that interlocus exchanges have played a structural role in the genesis of the human class I region.

L10 ANSWER 28 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95088094 EMBASE
TITLE: HLA class I chromosomal region, genes, and products: Facts and questions.
AUTHOR: Le Bouteiller P.
CORPORATE SOURCE: Unite INSERM 395, CHU Purpan, BP 3028, 31024 Toulouse, France
SOURCE: Critical Reviews in Immunology, (1994) 14/2 (89-129).
ISSN: 1040-8401 CODEN: CCRIDE
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Among the various areas of recent investigation in the field of human MHC class I antigens, the following have been selected for discussion in this review: (1) classical HLA class I genes: are they ubiquitously expressed?, what are the special features of their polymorphism?, are HLA-C molecules functional?, (2) non-classical HLA class I gene products: how restricted is their tissue distribution?, do they exhibit a little polymorphism?, what is their function, if any? (3) non-HLA genes recently detected in the HLA class I chromosomal region: are some of them involved in immunological function and development?, (4) other novel coding sequences present, or possibly present, in the region: the **hemochromatosis** gene, grc region and associated tumor suppressor genes, housekeeping genes, human equivalent of the murine H-2M region and Ped gene; (5) transcriptional regulation: are there cis-regulatory elements, including locus control region(s), located elsewhere than in the promoters? are CpG methylation, gene imprinting, chromatin structure, DNA rearrangement also implicated? what are the transcription factors involved and how do they interact with each other? is there HLA class I locus-, allele-, or isoform-specific regulation? is class I gene expression dysregulated in human tumors? The answers to these questions are crucial for the development of the future directions for research.

L10 ANSWER 29 OF 29 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90352719 EMBASE
TITLE: Molecular analysis of the human **MHC** class I region in hereditary haemochromatosis: A study by pulsed-field gel electrophoresis.
AUTHOR: Lord D.K.; Dunham I.; Campbell R.D.; Bomford A.; Strachan T.; Cox T.M.
CORPORATE SOURCE: Department of Medicine, University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, United Kingdom
SOURCE: HUM. GENET., (1990) 85/5 (531-536).
ISSN: 0340-6717 CODEN: HUGEDQ
COUNTRY: Germany, Federal Republic of
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
022 Human Genetics
LANGUAGE: English
AB The unknown allele that predisposes to the development of haemochromatosis in man has been localized to the HLA class I region on the short arm of chromosome 6. We have utilized pulsed-field gel electrophoresis in conjunction with probes that map within, or in the vicinity of, this region to search for structural lesions that may further define the disease locus. Using the enzyme Mlu I, fragments that associated specifically with the HLA-A23, A31 and B8 alleles were identified. However, in members of three pedigrees affected by haemochromatosis, and in six unrelated patients with the disorder, no disease-specific differences were detected in the DNA fragments with four restriction enzymes and eight probes when compared with healthy individuals. These data suggest that the lesion responsible for hereditary haemochromatosis lies beyond the resolution of this technique and does not involve large structural deletions or extensive re-arrangements in this highly polymorphic region of the genome.

=> file uspatfull

FILE 'USPATFULL' ENTERED AT 15:22:45 ON 17 FEB 1999
CA INDEXING COPYRIGHT (C) 1999 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 9 Feb 1999 (19990209/PD)
FILE LAST UPDATED: 10 Feb 1999 (19990210/ED)
HIGHEST PATENT NUMBER: US5870771
CA INDEXING IS CURRENT THROUGH 10 Feb 1999 (19990210/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 9 Feb 1999 (19990209/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: May 1998
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 1998

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>>> Image data for the /FA field are available the following week. <<<

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>>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<
>>> available for the WIPO International Patent Classification <<<
>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<
>>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<
>>> the /IC5 and /IC fields include the corresponding catchword <<<
>>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 15:06:12 ON 17 FEB 1999)

FILE 'MEDLINE, CANCERLIT, SCISEARCH, BIOSIS, EMBASE, WPIDS' ENTERED AT
15:06:39 ON 17 FEB 1999
SET PLURALS ON
L1 11342 S HEMOCHROMATOSIS
L2 252 S L1 AND MHC
L3 7 S L2 AND ALPHA-2
L4 5 DUP REM L3 (2 DUPLICATES REMOVED)
L5 4 S L2 AND ALPHA-3
L6 3 DUP REM L5 (1 DUPLICATE REMOVED)
L7 4 S L2 AND ALPHA-1
L8 4 DUP REM L7 (0 DUPLICATES REMOVED)
L9 36 S L1 AND MHC AND CLASS-1
L10 29 DUP REM L9 (7 DUPLICATES REMOVED)

FILE 'USPATFULL' ENTERED AT 15:22:45 ON 17 FEB 1999

=> s l9

79 HEMOCHROMATOSIS
1588 MHC
63 MHCS
1606 MHC
(MHC OR MHCS)
146795 CLASS
50776 CLASSES
168845 CLASS
(CLASS OR CLASSES)
2410805 1
2787 CLASS-1
(CLASS(W)1)
L11 0 L1 AND MHC AND CLASS-1

=> s l3

79 HEMOCHROMATOSIS
1588 MHC
63 MHCS
1606 MHC
(MHC OR MHCS)
266939 ALPHA
207 ALPHAS
266958 ALPHA
(ALPHA OR ALPHAS)
2409123 2
12198 ALPHA-2
(ALPHA(W)2)
L12 1 L2 AND ALPHA-2

=> d l12 ibib ab

L12 ANSWER 1 OF 1 USPATFULL
ACCESSION NUMBER: 97:91344 USPATFULL
TITLE: Methods to identify **hemochromatosis**
INVENTOR(S): Rothenberg, Barry E., P.O. Box 997, Del Mar, CA, United States 92014

	NUMBER	DATE
PATENT INFORMATION:	US 5674681	971007
APPLICATION INFO.:	US 94-349883	941206 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Horlick, Kenneth R.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 11

EXEMPLARY CLAIM: 2
LINE COUNT: 1877
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides methods to identify **hemochromatosis** in an individual. For example, the invention provides a method of detecting reduced association of .beta..sub.2 -microglobulin with a nonclassical **MHC** class I heavy chain molecule or a mutation in nonclassical **MHC** class I heavy chain-encoding DNA which results in a reduction of .beta..sub.2 -microglobulin-heavy chain association indicating that the individual tested has or is at risk of having **hemochromatosis**.

=> s l2

79 HEMOCHROMATOSIS
1588 MHC
63 MHCS
1606 MHC
(MHC OR MHCS)
L13 10 L1 AND MHC

=> d l13 1-10 ibib ab

L13 ANSWER 1 OF 10 USPATFULL
ACCESSION NUMBER: 1998:143661 USPATFULL
TITLE: Compositions and methods using complexes of heat shock proteins and antigenic molecules for the treatment and prevention of neoplastic diseases
INVENTOR(S): Srivastava, Pramod K., Riverdale, NY, United States
PATENT ASSIGNEE(S): Fordham University, Bronx, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5837251	981117
APPLICATION INFO.:	US 95-527391	950913 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Feisee, Lila
ASSISTANT EXAMINER: Bansal, Gee Tha D.
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1,8,16
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2361
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and compositions for eliciting an immune response and the prevention and treatment of primary and metastatic neoplastic diseases and infectious diseases. The methods of the invention comprise administering a composition comprising an effective amount of a complex, in which the complex consists essentially of a heat shock protein (hsp) noncovalently bound to an antigenic molecule. "Antigenic molecule" as used herein refers to the peptides with which the hsps are endogenously associated in vivo as well as exogenous antigens/immunogens (i.e., with which the hsps are not complexed in vivo) or antigenic/immunogenic fragments and derivatives thereof. In a preferred embodiment, the complex is autologous to the individual. The effective amounts of the complex are in the range of 10-600 micrograms for complexes comprising hsp70, 50-1000 micrograms for hsp90, and 10-600 micrograms for gp96. The invention also provides a method for measuring tumor rejection in vivo in an individual, preferably a human, comprising measuring the generation by the individual of **MHC** Class I-restricted CD8+ cytotoxic T lymphocytes specific to the tumor. Methods of purifying hsp70-peptide complexes are also provided.

L13 ANSWER 2 OF 10 USPATFULL
ACCESSION NUMBER: 1998:134628 USPATFULL
TITLE: Compositions and methods for the treatment and growth inhibition of cancer using heat shock/stress protein-peptide complexes in combination with adoptive immunotherapy
INVENTOR(S): Srivastava, Pramod K., Riverdale, NY, United States
PATENT ASSIGNEE(S): Fordham University, Bronx, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5830464	981103
APPLICATION INFO.:	US 97-796316	970207 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Saunders, David
ASSISTANT EXAMINER: VanderVegt, F. Pierre
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
LINE COUNT: 2332
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods and compositions for eliciting an immune response and the prevention and treatment of primary and metastatic neoplastic diseases and infectious diseases. The methods of the invention comprise administering a composition comprising an effective amount of a complex, in which the complex consists essentially of a heat shock protein (hsp) noncovalently bound to an antigenic molecule in combination with administering antigen presenting cells sensitized with complexes of hsps noncovalently bound to an antigenic molecule. "Antigenic molecule" as used herein refers to the peptides with which the hsps are endogenously associated in vivo as well as exogenous antigens/immunogens (i.e., with which the hsps are not complexed in vivo) or antigenic/immunogenic fragments and derivatives thereof. In a preferred embodiment, the complex is autologous to the individual. In a specific embodiment, the effective amounts of the complex when administered intradermally are in the range of 0.1 to 9.0 micrograms for complexes comprising hsp70, 5 to 49 micrograms for hsp90, and 0.1 to 9.0 micrograms for gp96. In another embodiment, the effective amounts of the complex when administered subcutaneously are in the range of 10 to 600 micrograms for complexes comprising hsp70, 50 to 5000 micrograms for hsp90, and 10 to 600 micrograms for gp96.

L13 ANSWER 3 OF 10 USPATFULL
ACCESSION NUMBER: 97:104495 USPATFULL
TITLE: Aminomethylene derivaties as immunosuppressants
INVENTOR(S): Connell, Richard D., New Haven, CT, United States
Osterman, David G., Glastonbury, CT, United States
Katz, Michael E., Wallingford, CT, United States
Dally, Robert D., Branford, CT, United States
PATENT ASSIGNEE(S): Miles Inc., West Haven, CT, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5686469	971111
APPLICATION INFO.:	US 95-571028	951212 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 93-15703, filed on 9 Feb 1993, now patented, Pat. No. US 5385918
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Chang, Ceila
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
LINE COUNT: 1474
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds which suppress human T-lymphocyte proliferation are disclosed.
The active compounds essentially contain at least the following structure: ##STR1##

L13 ANSWER 4 OF 10 USPATFULL
ACCESSION NUMBER: 97:104454 USPATFULL
TITLE: 2-oxoethyl derivatives as immunosuppressants
INVENTOR(S): Connell, Richard D., New Haven, CT, United States
Osterman, David G., Glastonbury, CT, United States
Katz, Michael E., Wallingford, CT, United States
PATENT ASSIGNEE(S): Miles Inc., West Haven, CT, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5686424	971111
APPLICATION INFO.:	US 95-431390	950428 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 92-981565, filed on 25 Nov 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-864998, filed on 8 Apr 1992, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Gerstl, Robert
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 3158
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A class of compounds that suppress human T-lymphocyte proliferation is disclosed. The active compounds essentially contain at least the following structure: ##STR1##

L13 ANSWER 5 OF 10 USPATFULL
ACCESSION NUMBER: 97:91344 USPATFULL
TITLE: Methods to identify **hemochromatosis**
INVENTOR(S): Rothenberg, Barry E., P.O. Box 997, Del Mar, CA, United States 92014

	NUMBER	DATE
PATENT INFORMATION:	US 5674681	971007
APPLICATION INFO.:	US 94-349883	941206 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Horlick, Kenneth R.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 2
LINE COUNT: 1877
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides methods to identify **hemochromatosis** in an individual. For example, the invention provides a method of detecting reduced association of .beta..sub.2 -microglobulin with a nonclassical **MHC** class I heavy chain molecule or a mutation in nonclassical **MHC** class I heavy chain-encoding DNA which results in a reduction of .beta..sub.2 -microglobulin-heavy chain association indicating that the individual tested has or is at risk of having **hemochromatosis**.

L13 ANSWER 6 OF 10 USPATFULL
ACCESSION NUMBER: 97:52184 USPATFULL
TITLE: Chimeric immunocompromised mammal comprosing vascularized fetal organ tissue
INVENTOR(S): McCune, III, Joseph M., San Francisco, CA, United States
PATENT ASSIGNEE(S): The Board of Trustees for the Leland Stanford Junior University, Palo Alto, CA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5639939	970617
APPLICATION INFO.:	US 94-205053	940301 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 91-737882, filed on 25 Jul 1991, now abandoned which is a continuation of Ser. No. US 89-343797, filed on 26 Apr 1989, now abandoned which is a continuation-in-part of Ser. No. US 88-287075, filed on 20 Dec 1988, now abandoned which is a continuation of Ser. No. US 87-137173, filed on 23 Dec 1987, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Chambers, Jasemine C.
ASSISTANT EXAMINER: Schmuck, Jill
LEGAL REPRESENTATIVE: Sherwood, Pamela J.Fish and Richardson P.C.
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 6
LINE COUNT: 1597
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Xenogeneic tissue is introduced into an immunocompromised host for interacting with agents and using such interaction for evaluating efficacy of drugs and vaccines, producing xenogeneic monoclonal antibodies, evaluating the effect of the various agents on specific tissues and the like. Particularly, drugs can be evaluated for their efficacy against a wide variety of pathogens which infect xenogeneic

tissue, agents can be evaluated for their effect on the xenogeneic immune system and monoclonal antibodies to a predetermined epitope may be produced.

L13 ANSWER 7 OF 10 USPATFULL
ACCESSION NUMBER: 97:45039 USPATFULL
TITLE: Sulfonamide aminomethylene derivatives as immunosuppressants
INVENTOR(S): Connell, Richard D., New Haven, CT, United States
Osterman, David G., Glastonbury, CT, United States
Katz, Michael E., Wallingford, CT, United States
Daily, Robert D., Branford, CT, United States
PATENT ASSIGNEE(S): Miles Inc., West Haven, CT, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5633277	970527
APPLICATION INFO.:	US 95-535507	950926 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 93-15502, filed on 9 Feb 1993, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Wu, Shean C.
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 1014
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds which suppress human T-lymphocyte proliferation are disclosed.
The active compounds essentially contain at least the following structure: ##STR1##

L13 ANSWER 8 OF 10 USPATFULL
ACCESSION NUMBER: 95:9709 USPATFULL
TITLE: Aminomethylene-peptides as immunosuppressants
INVENTOR(S): Connell, Richard D., New Haven, CT, United States
Osterman, David G., Glastonbury, CT, United States
Katz, Michael E., Wallingford, CT, United States
Hanko, Rudolf, Essen, Germany, Federal Republic of
Schneider, Stephan, Madison, CT, United States
PATENT ASSIGNEE(S): Miles Inc., West Haven, CT, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5385918	950131
APPLICATION INFO.:	US 93-15688	930209 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Chang, Celia
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
LINE COUNT: 1210
AB Compounds which suppress human T-lymphocyte proliferation are disclosed.
The active compounds essentially contain at least the following structure: ##STR1## wherein A, R.sup.1, R.sup.2, R.sup.3, n, X.sup.1 and Z are defined in the specification.

L13 ANSWER 9 OF 10 USPATFULL
ACCESSION NUMBER: 93:18461 USPATFULL
TITLE: Isolation and preservation of fetal and neonatal hematopoietic stem and progenitor cells of the blood and methods of therapeutic use
INVENTOR(S): Boyse, Edward A., Tucson, AZ, United States
Broxmeyer, Hal E., Indianapolis, IN, United States
Douglas, Gordon W., New York, NY, United States
PATENT ASSIGNEE(S): Biocyte Corporation, New York, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5192553	930309
APPLICATION INFO.:	US 88-269926	881110 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 87-119746, filed on 12 Nov 1987, now patented, Pat. No. US 5004681
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rosen, Sam
NUMBER OF CLAIMS: 64
EXEMPLARY CLAIM: 1,13,47
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 3392
AB The present invention relates to hematopoietic stem and progenitor cells of neonatal or fetal blood that are cryopreserved, and the therapeutic uses of such stem and progenitor cells upon thawing. In particular, the present invention relates to the therapeutic use of fetal or neonatal stem cells for hematopoietic (or immune) reconstitution. Hematopoietic reconstitution with the cells of the invention can be valuable in the treatment or prevention of various diseases and disorders such as anemias, malignancies, autoimmune disorders, and various immune dysfunctions and deficiencies. In another embodiment, fetal or neonatal hematopoietic stem and progenitor cells which contain a heterologous gene sequence can be used for hematopoietic reconstitution in gene therapy. In a preferred embodiment of he invention, neonatal or fetal blood cells that have been cryopreserved and thawed can be used for utologous (self) reconstitution.

L13 ANSWER 10 OF 10 USPATFULL
ACCESSION NUMBER: 91:26556 USPATFULL
TITLE: Preservation of fetal and neonatal hematopoietic stem and progenitor cells of the blood
INVENTOR(S): Boyse, Edward A., New York, NY, United States
Broxmeyer, Hal E., Indianapolis, IN, United States
Douglas, Gordon W., New York, NY, United States
PATENT ASSIGNEE(S): Biocyte Corporation, New York, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5004681	910402
APPLICATION INFO.:	US 87-119746	871112 (7)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Rosen, Sam
LEGAL REPRESENTATIVE: Pennie & Edmonds
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 3099
AB The present invention relates to hematopoietic stem and progenitor cells of neonatal or fetal blood that are cryopreserved, and the therapeutic uses of such stem and progenitor cells upon thawing. In particular, the present invention relates to the therapeutic use of fetal or neonatal stem cells for hematopoietic (or immune) reconstitution. Hematopoietic reconstitution with the cells of the invention can be valuable in the treatment or prevention of various diseases and disorders such as anemias, malignancies, autoimmune disorders, and various immune dysfunctions and deficiencies. In another embodiment, fetal or neonatal hematopoietic stem and progenitor cells which contain a heterologous gene sequence can be used for hematopoietic reconstitution in gene therapy. In a preferred embodiment of the invention, neonatal or fetal blood cells that have been cryopreserved and thawed can be used for autologous (self) reconstitution.

=> d his

(FILE 'HOME' ENTERED AT 15:06:12 ON 17 FEB 1999)

FILE 'MEDLINE, CANCERLIT, SCISEARCH, BIOSIS, EMBASE, WPIDS' ENTERED AT 15:06:39 ON 17 FEB 1999
SET PLURALS ON
L1 11342 S HEMOCHROMATOSIS
L2 252 S L1 AND MHC
L3 7 S L2 AND ALPHA-2
L4 5 DUP REM L3 (2 DUPLICATES REMOVED)
L5 4 S L2 AND ALPHA-3
L6 3 DUP REM L5 (1 DUPLICATE REMOVED)
L7 4 S L2 AND ALPHA-1
L8 4 DUP REM L7 (0 DUPLICATES REMOVED)
L9 36 S L1 AND MHC AND CLASS-1
L10 29 DUP REM L9 (7 DUPLICATES REMOVED)

FILE 'USPATFULL' ENTERED AT 15:22:45 ON 17 FEB 1999
L11 0 S L9
L12 1 S L3
L13 10 S L2

=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

STN INTERNATIONAL LOGOFF AT 15:28:38 ON 17 FEB 1999